

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PATENT
Docket No.: 026549-000100US
Client Ref. No.: 30836

On _____

TOWNSEND and TOWNSEND and CREW LLP

By: _____

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Ronit Eisenberg

Patent No.:

Issued:

Application No.: 10/009,809

Filed: April 26, 2002

For: CELL PENETRATING ANTI-ALLERGIC PEPTIDES

Confirmation No.: 1519

Examiner: Crowder, Chun

Art Unit: 1644

RULE 132 DECLARATION

Commissioner
P.O.
Alexandria, VA 22313-1450

for
Box

Patents
1450

Sir:

I, Dr. Ehud Razin, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. § 1001, and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true and statements made on information or belief are believed to be true. The Exhibits (1 and _ attached hereto are incorporated herein by reference.

2. I received a Ph.D. in Immunology/Cell Biology from the Weizmann Institute of Science in 1980.

A copy of my curriculum vitae is attached as Exhibit 1.

3. I am presently employed at the Hebrew University of Jerusalem and am primarily responsible for teaching and research.

4. I have read and am familiar with the contents of the application. I understand that the Examiner has a single rejection based on obviousness that is based on a combination of three references. The references are Holgate as a primary reference in view of Aridor and Lin. Holgate is cited as disclosing that agents that inhibit mast cell degranulation are recognized for treatment of diseases such as asthma. Aridor discloses KNNLKECGLY which is a mast cell activation inhibitor designated Gai3 C-terminal peptide. Lin discloses the preferred cell penetrating peptide from Kaposi fibroblast growth factor [KFGF].

5. This invention is the surprising discovery that of four different cell penetrating peptides (CCP) only one CCP was able to successfully deliver two mast cell activation inhibitors in a biologically active manner. Because the prior art literature would suggest to those of skill that CCPs are interchangeable, it is surprising that the choice of CCP would be critical for obtaining biological activity. Accordingly, we have to conclude that the field of using cell penetrating peptides to deliver biologically active proteins is far less predictable than the Examiner believes it to be and that the applicants' results as embodied in the pending claims are both surprising and advantageous..

The following statements provide objective, scientific reasons for the above conclusion.

6. It is my understanding that the rejection of the pending claims is based on the proposition that Lin's teaching of the CCP, (AAVALLPAVLLALLAP) as a tool for delivery of biologically active cargo peptides renders the claimed combinations of AAVALLPAVLLALLAP in reading frame fusions with Gai₃ or Gat C-terminal peptides obvious and unpatentable. In brief, the Examiner believes that upon reading the three references, one of skill would be motivated by Holgate to combine the KFGF CCP of Lin with the mast cell activation inhibitor of Aridor, Gai₃, with a reasonable expectation that the combination would inhibit mast cell activation.

It is also my understanding that evidence of unpredictability or surprising results can legally refute this conclusion and lead to the rejection being withdrawn.

It is my further opinion that both unpredictability and surprising results have been demonstrated by the applicants' work and by the literature already of record.

7. More specifically, we know that of the four CCPs tested only one CCP was able to deliver the two mast cell activation inhibitors, Gai₃ or Gat, as a biologically active inhibitors. The table below summarizes Applicants' results as described in the specification and in the Jones et al. publication.

CHIMERIC PEPTIDE

RESULTS

Hu Int	Gai ₃	SEQ ID NO: 6	No inhibition of histamine secretion
KFGF	Gai ₃	SEQ ID NO: 7	Inhibited histamine secretion
Dros	Gai ₃	SEQ ID NO: 10	Induced histamine

			secretion
Hu Int	Gat	SEQ ID NO: 11	No inhibition of histamine secretion
KFGF SEQ ID NO: 3	Gat	SEQ ID NO: 12	Inhibited histamine secretion
Dros	Gat	SEQ ID NO: 13	Induced histamine secretion
TP-10	Gat ₃	Jones <i>et al.</i>	No inhibition of beta-hexoseaminidase secretion

8. From this data, it is clear that only Lin's CCP, KFGF is able to both deliver mast cell activation inhibitors and maintain their biological activity as inhibitors of mast cell activation. The Examiner says that this is predictable from the literature. I respectfully disagree.

Lin discloses that KFGF sequence transported two biologically active cargo peptides and generally states that KFGF can be used to transport other peptides. But similar reports exist for each of the other CCPs tested by applicants. The Hawiger review article discloses that the CCP designated integrin β_3 is just as able as KFGF to transport functional peptides into a cell (see page 189, 2nd column). Finally Derossi *et al.* describes the *Drosophila* CCP as successfully delivering biologically active compounds inside live cells (page 18188, 2nd col).

From page 7 of the Office Action, the Examiner appears to interpret this literature as leading one of skill to believe that there is a reasonable expectation that any

combination of CCP with any biologically active peptide will lead to the observation of biological activity in a cell.

I respectfully disagree. There are several scientific and objective reasons why fusing a CCP to a biologically active peptide might not result in observation of expected biological activity. These reasons include improper folding of the fusion peptide resulting in conformational changes that render the cargo peptide inactive; the degradation of the foreign peptide; sequestering of the peptide in endosomes or the ability of the CCP sequence to trigger a biological response, such as mast cell degranulation (e.g. positively charged CCP might function as basic secretagogues of mast cells).

Indeed, this appears to be the case for fusion of CCP with either Gai₃ or Gat. The data from applicants' laboratory and from the Jones *et al.* group demonstrate that not any CCP can maintain the biological activity of Gai₃ or Gat. Of four CCPs, only KFGF was the only CCP able to both internalize and maintain the inhibitory activity of both Gai₃ and Gat. Thus the combination provides a surprisingly advantageous result that was not predictable from the prior art.

I do note the Examiner's statement on page 7 that the table on page 9 with reference to the prior literature describing the various CCPs fail to demonstrate that Lin's CCP is unpredictable as a delivery tool. While this is true, there was no academic reason *a priori* to believe that any of the other CCPs would fail to deliver Gai₃ and Gat while maintaining its expected biological activity. But the evidence established by the record indicates that this is not true. There is obviously something special about the two mast cell activation inhibitors or with Lin's CCP that makes the claimed combination functional compared to the other three CCPs.

For these reasons, I conclude without hesitation that the claimed combinations of AAVALLPAVLLALLAP with either Gui_3 or Gat to yield a functional inhibitory effect on mast cell activation in light of failure with three other CCPs of equal status was unpredictable, surprising and of great value.

This Declarant has nothing further to say.

Dated: May 6 2007

Dr. Ehud Razin Ehud Razin

TOWNSEND
Two
San
Tel:
Fax:
KAW:kaw
61036970

and
Embarcadero
Francisco,

TOWNSEND
Center,
California
(415)
(415)

and CREW
Eighth

LLP
Floor
94111-3834
576-0200
576-0300

CURRICULUM VITAE

Name: Ehud Razin
Birthdate: July 14, 1947
Marital Status: Married (Michal), two children: Ayelet (1979),
Jonatan (1986).
Title: Professor of Biochemistry, Hebrew-University,
Hadassah Medical School.
Dr. Marcus Rabwin Chair in Cancer Research

Research Interests: Biology of Mast Cells

EDUCATION:

1965 - 1968 Captain, Israeli Army
1970 - 1973 B. Sc. Biology - Hebrew University of Jerusalem
1973 - 1975 M. Sc. Microbiology - Hebrew University of
Jerusalem
1976 - 1980 Ph.D. Immunology - Weizmann Institute of Science

PROFESSIONAL EXPERIENCE:

2005- Dean Faculty of Medicine Hebrew University
2001-2005 Chairman of the Faculty's Planning &
Development Committee
1998-2001 Chairman Biochemistry Department
1996- Professor of Biochemistry
1997-8 Visiting Scientist of NIAMS, NIH
1993 July-December Visiting Scientist, NIH, U.S.A.

1991-1996 Assoc. Professor in Biochemistry, Hebrew University
of Jerusalem
1987 - 1991 Senior Lecturer in Biochemistry, Hebrew University of
Jerusalem.
1983 - 1987 Lecturer in Biochemistry, Hebrew University of
Jerusalem.
1982 - 1984 Research Fellow - Immunopharmacology, Harvard
Medical School, Boston, MA, USA.
1980 - 1981 Research Fellow - Immunology, Memorial Sloan-
Kettering Cancer Centre, NY, USA.
1989 - 1990 Visiting Professor, Biomedical Research Centre, UBC,
Vancouver, Canada.
1987 - 1989 Consultant, Syntex Research Co., Palo Alto, CA, USA

AWARDS:

1979 DAAD Scholarship
1980 Chaim Weizmann Fellowship

SOCIETIES:

1983 American Association of Immunologists

1994 CoLLEGIUM INTERNATIoNALE
ALLERGoLoGICUM (CIA).
1998 American Society for Biochemistry and Molecular
Biology.

Ehud Razin:

Publications

1. Razin, E., Bauminger, S., Globerson, A. Effect of prostaglandins on phagocytosis of sheep erythrocytes by mouse peritoneal macrophages. *J Reticuloendothel Soc* 1978; 23: 237-42.
 2. Razin, E., Zor, U., Globerson, A. Function of macrophage prostaglandins in the process of phagocytosis. *Adv Exp Med Biol* 1979; 121: 413-7.
 3. Razin, E., Globerson, A. The effect of various prostaglandins on plasma membrane receptors and function of mouse macrophages. *Adv Exp Med Biol* 1979; 114: 415-9.
 4. Razin, E., Razin, M., Lohmann-Matthes, M.L. The role of prostaglandins in the development of macrophages from bone marrow cells. *J Reticuloendothel Soc* 1980; 27: 377-82.
 5. Razin, E., Rivnay, B., Globerson, A. Prostaglandins as modulators of macrophage development from bone marrow. *J Reticuloendothel Soc* 1981; 30: 239-46.
 6. Razin, E., Rifkind, A.B., Cordon-Cardo, C., Good, R.A. Selective growth of a population of human basophil cells in vitro. *Proc Natl Acad Sci U S A* 1981; 78: 5793-6.
 7. Razin, E., Hayari, Y., Globerson, A. Effects of indomethacin on hematopoiesis in mice. *Prostaglandins Med* 1981; 6: 613-20.
 8. Razin, E., Klein, B., Globerson, A. Effects of indomethacin treatment of human peripheral blood monocytes. *Prostaglandins Med* 1981; 6: 529-36.
 9. Razin, E., Cordon-Cardo, C., Good, R.A. Growth of a pure population of mouse mast cells in vitro with conditioned medium derived from concanavalin A-stimulated splenocytes. *Proc Natl Acad Sci U S A* 1981; 78: 2559-61.
 10. Razin, E., Mencia-Huerta, J.M., Lewis, R.A., Corey, E.J., Austen, K.F. Generation of leukotriene C4 from a subclass of mast cells differentiated in vitro from mouse bone marrow. *Proc Natl Acad Sci U S A* 1982; 79: 4665-7.
 11. Razin, E., Cordon-Cardo, A., Minick, C.R., Good, R.A. Studies on the exocytosis of cultured mast cells derived from mouse bone marrow. *Exp Hematol* 1982; 10: 524-32.
 12. Razin, E., Stevens, R.L., Akiyama, F., Schmid, K., Austen, K.F. Culture from mouse bone marrow of a subclass of mast cells possessing a distinct chondroitin sulfate proteoglycan with glycosaminoglycans rich in N-acetylgalactosamine-4,6-disulfate. *J Biol Chem* 1982; 257: 7229-36.
 13. Razin, E., Globerson, A., Skutelsky, E. Indomethacin modulates plasma membrane-associated properties of macrophages. *Prostaglandins Leukot Med* 1982; 8: 301-10.
 14. Mencia-Huerta, J.M., Lewis, R.A., Razin, E., Austen, K.F. Antigen-initiated release of platelet-activating factor (PAF-acether) from mouse bone marrow-derived mast cells sensitized with monoclonal IgE. *J Immunol* 1983; 131: 2958-64.
 15. Mencia-Huerta, J.M., Razin, E., Ringel, E.W., Corey, E.J., Hoover, D., Austen, K.F., et al. Immunologic and ionophore-induced generation of leukotriene B4 from mouse bone marrow-derived mast cells. *J Immunol* 1983; 130: 1885-90.
 16. Razin, E., Mencia-Huerta, J.M., Stevens, R.L., Lewis, R.A., Liu, F.T., Corey, E., et al. IgE-mediated release of leukotriene C4, chondroitin sulfate E proteoglycan, beta-hexosaminidase, and histamine from cultured bone marrow-derived mouse mast cells. *J Exp Med* 1983; 157: 189-201.
 17. Stevens, R.L., Razin, E., Austen, K.F., Hein, A., Caulfield, J.P., Seno, N., et al. Synthesis of chondroitin sulfate E glycosaminoglycan onto p-nitrophenyl-beta-D-xyloside and its localization to the secretory granules of rat serosal mast cells and mouse bone marrow-derived mast cells. *J Biol Chem* 1983; 258: 5977-84.
-

18. Razin, E., Marx, G. Thrombin-induced degranulation of cultured bone marrow-derived mast cells. *J Immunol* 1984; 133: 3282-5.
19. Razin, E., Romeo, L.C., Krilis, S., Liu, F.T., Lewis, R.A., Corey, E.J., et al. An analysis of the relationship between 5-lipoxygenase product generation and the secretion of preformed mediators from mouse bone marrow-derived mast cells. *J Immunol* 1984; 133: 938-45.
20. Razin, E., Stevens, R.L., Austen, K.F., Caulfield, J.P., Hein, A., Liu, F.T., et al. Cloned mouse mast cells derived from immunized lymph node cells and from foetal liver cells exhibit characteristics of bone marrow-derived mast cells containing chondroitin sulphate E proteoglycan. *Immunology* 1984; 52: 563-75.
21. Razin, E., Ihle, J.N., Seldin, D., Mencia-Huerta, J.M., Katz, H.R., LeBlanc, P.A., et al. Interleukin 3: A differentiation and growth factor for the mouse mast cell that contains chondroitin sulfate E proteoglycan. *J Immunol* 1984; 132: 1479-86.
22. Stevens, R.L., Bloes, W.F., Seldin, D.C., Razin, E., Katz, H.R., Austen, K.F. Inhibition of proliferation of mouse T cell-dependent bone marrow-derived mast cells by rat serum does not change their unique phenotype. *J Immunol* 1984; 132: 2674-80.
23. Pervin, R., Kanner, B.I., Marx, G., Razin, E. Thrombin-induced degranulation of cultured bone marrow-derived mast cells: effect on calcium uptake. *Immunology* 1985; 56: 667-72.
24. Razin, E., Baranes, D., Marx, G. Thrombin-mast cell interactions. Binding and cell activation. *Exp Cell Res* 1985; 160: 380-6.
25. Razin, E. Activation of the 5-lipoxygenase pathway in E-mast cells by peanut agglutinin. *J Immunol* 1985; 134: 1142-5.
26. Shoam, H., Razin, E. BW755C inhibits the 5-lipoxygenase in E-mast cells without affecting degranulation. *Biochim Biophys Acta* 1985; 837: 1-5.
27. Baranes, D., Matzner, J., Razin, E. Thrombin-induced calcium-independent degranulation of human neutrophils. *Inflammation* 1986; 10: 455-61.
28. Baranes, D., Liu, F.T., Razin, E. Thrombin and IgE antigen induce formation of inositol phosphates by mouse E-mast cells. *FEBS Lett* 1986; 206: 64-8.
29. Baranes, D., Liu, F.T., Marx, G., Shalit, M., Razin, E. Regulation of thrombin-induced mast cell degranulation by zinc and manganese. *Immunol Lett* 1986; 12: 95-9.
30. Eliakim, R., Gilead, L., Ligumsky, M., Okon, E., Rachmilewitz, D., Razin, E. Histamine and chondroitin sulfate E proteoglycan released by cultured human colonic mucosa: indication for possible presence of E mast cells. *Proc Natl Acad Sci U S A* 1986; 83: 461-4.
31. Razin, E., Baranes, D. Thrombin-induced lysozyme release from human neutrophils and phosphatidylinositol breakdown in cultured mouse E mast cells. *Adv Prostaglandin Thromboxane Leukot Res* 1986; 16: 135-40.
32. Shalit, M., Shoam, H., Seno, N., Razin, E. New role for heparan sulfate: regulator of leukotriene generation in mouse E-mast cells. *Life Sci* 1986; 39: 903-10.
33. Gilead, L., Livni, N., Eliakim, R., Ligumsky, M., Fich, A., Okon, E., Rachmilewitz, D., Razin, E. Human gastric mucosal mast cells are chondroitin sulphate E-containing mast cells. *Immunology* 1987; 62: 23-8.
34. Lerner, M., Samuni, A., Razin, E. Stimulation of murine cultured mast cells under anaerobic conditions: inhibition of arachidonic acid release. *Immunol Lett* 1987; 16: 121-4.
35. Eliakim, R., Karmeli, F., Razin, E., Rachmilewitz, D. Role of platelet-activating factor in ulcerative colitis. Enhanced production during active disease and inhibition by sulfasalazine and prednisolone. *Gastroenterology* 1988; 95: 1167-72.
36. Gilead, L., Rahamim, E., Ziv, L., Or, R., Razin, E. Cultured human bone marrow-derived mast cells, their similarities to cultured murine E-mast cells. *Immunology* 1988; 63: 669-75.
37. Matzner, Y., Cohn, M., Hyam, E., Razin, E., Fuks, Z., Buchanan, M.R., et al. Generation of lipid neutrophil chemoattractant by irradiated bovine aortic endothelial cells. *J Immunol* 1988; 140: 2681-5.

38. Bashkin, P., Razin, E., Eldor, A., Vlodavsky, I. Degranulating mast cells secrete an endoglycosidase that degrades heparan sulfate in subendothelial extracellular matrix. *Blood* 1990; 75: 2204-12.
39. Chaikin, E., Ziltener, H.J., Razin, E. Protein kinase C plays an inhibitory role in interleukin 3- and interleukin 4-mediated mast cell proliferation. *J Biol Chem* 1990; 265: 22109-16.
40. Davidson, S., Gilead, L., Amira, M., Ginsburg, H., Razin, E. Synthesis of chondroitin sulfate D and heparin proteoglycans in murine lymph node-derived mast cells. The dependence on fibroblasts. *J Biol Chem* 1990; 265: 12324-30.
41. Gilead, L., Bibi, O., Razin, E. Fibroblasts induce heparin synthesis in chondroitin sulfate E containing human bone marrow-derived mast cells. *Blood* 1990; 76: 1188-95.
42. Razin, E. Culture of bone marrow-derived mast cells: a model for studying oxidative metabolism of arachidonic acid and synthesis of other molecules derived from membrane phospholipids. *Methods Enzymol* 1990; 187: 514-20.
43. Baranes, D., Razin, E. Protein kinase C regulates proliferation of mast cells and the expression of the mRNAs of fos and jun proto-oncogenes during activation by IgE-Ag or calcium ionophore A23187. *Blood* 1991; 78: 2354-64.
44. Razin, E., Leslie, K.B., Schrader, J.W. Connective tissue mast cells in contact with fibroblasts express IL-3 mRNA. Analysis of single cells by polymerase chain reaction. *J Immunol* 1991; 146: 981-7.
45. Baranes, D., Lewin, I., Razin, E. Serum modulates mast cell responses to IgE antigen stimulation. *Eur J Immunol* 1993; 23: 291-4.
46. Lewin, I., Nechushtan, H., Ke, Q., Razin, E. Regulation of AP-1 expression and activity in antigen-stimulated mast cells: the role played by protein kinase C and the possible involvement of Fos interacting protein. *Blood* 1993; 82: 3745-51.
47. Ophir, A., Berenshtein, E., Ziltener, H.J., Razin, E. 5-fluorouracil and mast cell precursors in mice. *Exp Hematol* 1993; 21: 1558-62.
48. Chaikin, E., Hakeem, I., Razin, E. Enhancement of interleukin-3-dependent mast cell proliferation by suppression of c-jun expression. *J Biol Chem* 1994; 269: 8498-503.
49. Razin, E., Szallasi, Z., Kazanietz, M.G., Blumberg, P.M., Rivera, J. Protein kinases C-beta and C-epsilon link the mast cell high-affinity receptor for IgE to the expression of c-fos and c-jun. *Proc Natl Acad Sci U S A* 1994; 91: 7722-6.
50. Chaikin, E., Hakeem, I., Razin, E. The incapability of interleukin-4 to induce AP-1 activity in murine mast cells. *Int Arch Allergy Immunol* 1995; 107: 57-9.
51. Cruz, J.R., Cano, F., Razin, E., Acheson, D.W., Keusch, G.T. Fecal excretion of leukotriene C4 during human disease due to *Shigella dysenteriae*. *J Pediatr Gastroenterol Nutr* 1995; 20: 179-83.
52. Razin, E., Pecht, I., Rivera, J. Signal transduction in the activation of mast cells and basophils. *Immunol Today* 1995; 16: 370-3.
53. Lewin, I., Jacob-Hirsch, J., Zang, Z.C., Kupershtein, V., Szallasi, Z., Rivera, J., Razin, E. Aggregation of the FcεRI in mast cells induces the synthesis of Fos-interacting protein and increases its DNA binding-activity: the dependence on protein kinase C-beta. *J Biol Chem* 1996; 271: 1514-9.
54. Nechushtan, H., Razin, E. Regulation of mast cell growth and proliferation. *Crit Rev Oncol Hematol* 1996; 23: 131-50.
55. Nechushtan, H., Soreq, H., Kuperstein, V., Tshori, S., Razin, E. Murine and human mast cell express acetylcholinesterase. *FEBS Lett* 1996; 379: 1-6.
56. Ligumsky, M., Kuperstein, V., Nechushtan, H., Zhang, Z., Razin, E. Analysis of cytokine profile in human colonic mucosal Fc epsilonRI-positive cells by single cell PCR: inhibition of IL-3 expression in steroid-treated IBD patients. *FEBS Lett* 1997; 413: 436-40.

57. Nechushtan, H., Zhang, Z., Razin, E. Microphthalmia (mi) in murine mast cells: regulation of its stimuli-mediated expression on the translational level. *Blood* 1997; 89: 2999-3008.
58. Frenkel, S., Kay, G., Nechushtan, H., Razin, E. Nuclear translocation of upstream stimulating factor 2 (USF2) in activated mast cells: a possible role in their survival. *J Immunol* 1998; 161: 2881-7.
59. Nechushtan, H., Razin, E. Deciphering the early-response transcription factor networks in mast cells. *Immunol Today* 1998; 19: 441-4.
60. Zhang, Z.C., Nechushtan, H., Jacob-Hirsch, J., Avni, D., Meyuhas, O., Razin, E. Growth-dependent and PKC-mediated translational regulation of the upstream stimulating factor-2 (USF2) mRNA in hematopoietic cells. *Oncogene* 1998; 16: 763-9.
61. Nechushtan, H., Razin, E. Early-Response genes in mast cell activation. In: *Razin, E., Rivera, J., eds. *Signal transduction in mast cells and basophils*. New York Berlin Heidelberg: Springer-Verlag, 1999; Section 4: 323-7.
62. Razin, E., Zhang, Z.C., Nechushtan, H., Frenkel, S., Lee, Y.N., Arudchandran, R., et al. Suppression of microphthalmia transcriptional activity by its association with protein kinase C-interacting protein 1 in mast cells. *J Biol Chem* 1999; 274: 272-6-274 ;
63. Bauer, O., Razin, E. Mast Cell-Nerve Interactions. *News Physiol Sci* 2000; 15: 213-8.
64. Frenkel, S., Kay, G., Razin, E. Early response transcription factors in activated mast cells. *MAI* 2000; 1: 57-8.
65. Nechushtan, H., Leitges, M., Cohen, C., Kay, G., Razin, E. Inhibition of degranulation and interleukin-6 production in mast cells derived from mice deficient in protein kinase C β . *Blood* 2000; 95: 1752-7.
66. Nechushtan, H., Razin, E. Studies of different aspects of the role of protein kinase C in mast cells. *Int Arch Allergy Immunol* 2001; 124: 130-2.
67. Levy, C., Nechushtan, H., Razin, E. A new role for the STAT3 inhibitor, PIAS3: a repressor of microphthalmia transcription factor. *J Biol Chem* 2002; 277: 1962-6.
68. Nechushtan, H., Razin, E. The function of MITF and associated proteins in mast cells. *Mol Immunol* 2002; 38: 1177.
69. Cohen-Saidon, C., Nechushtan, H., Kahlon, S., Livni, N., Nissim, A., Razin E. A novel strategy using single chain antibody to show the importance of Bcl-2 in mast cell survival. *Blood* 2003; 102: 2056.
70. Levy, C., Sonnenblik, A., Razin, E. Phosphorylation and the Zip domain of MITF play a role in its transcriptional inhibition by PIAS3. *Mol Cell Biol* 2003; 23: 9073.
71. * Lee, Y.N., Nechushtan, H., Figov, N., Razin, E. The function of lysyl-tRNA synthetase and Ap4A as signaling regulators of MITF activity in Fc ϵ RI-activated mast cells. *Immunity* 2004; 20: 145-51.
72. Lee, Y.-N., Tuckerman, J., Nechushtan, H., Schutz, G., Razin*, E., Angel, P. c-Fos as a regulator of degranulation and cytokine production in Fc ϵ RI activated mast cells. *J. Immunol.* 2004; 173: 2571-7.
73. Sonnenblik, A., Levy, C., Razin, E. Interplay between MITF, PIAS3, and STAT3 in Mast Cells and Melanocytes. *Mol Cell Biol* 2004; 24: 10584-92.
74. Miller, A.J., Levy, C., Davis, I.J., Razin, E., Fisher, D.E. Sumoylation of MITF and its related family members TFE3 and TFEB. *J Biol Chem* 2005; 280: 146-55.
75. Sonnenblik, A., Levy, C., Razin, E. Regulation of MITF and STAT3 in mast cells by monomeric IgE .. *J of Immunology* 2005; 175: 1450-1455.
76. Lee, Y and Razin, E. The non-conventional involvement of LysRS in molecular mechanism of USF2 transcriptional activity in activated Fc ϵ RI mast cells. *Mol Cell Biol* . 2005 25: 8904_ 8912.

77. Cohen-Saidon, C; Carmi, I; Keren, A and Razin E; The anti-apoptotic function of Bcl-2 in mast cells is dependent on its association with Heat Shock Protein 90 β . Blood 2006 107: 1413-1420.
78. Levy, C; Lee, Y-N; Nechushtan, H; Sonnenblick, A; Schueler-Furman, O; Hacohen S and Razin, E. Short PIAS3 motif interferes with transcriptional activity of MITF and STAT3 in mast cells and melanocytes" Blood 2006 107: 2839-2845.
79. Cohen-Saidon C and Razin, E. The involvement of Bcl-2 in mast cell apoptosis. In "Mast Cell and Basophils: Development activation and role in allergic/autoimmune disease. Novartis Foundation Symposium 271. 2006 WILEY. P191-197.
80. Nechushtan, H and Razin, E. Mast cells: must they always be different? 2006 Blood 107: 1-2.
81. ** Tshori, S; Gilon, D; Beeri, R; Nechushtan, H; Kaluzhny, D; Pikarsky, E and Razin, Ehud. The transcription factor MITF regulates cardiac growth and hypertrophy. Journal of Clinical Investigation., 2006, 116:2673-2681.
82. The microphthalmia transcription factor isoforms in mast cells and in the heart: Sagi Tshori; Amir Sonnenblick; Nurit Yanay-Cohen; Gillian Kay; Hovav Nechushtan and Ehud Razin. 2007 Molecular and Cellular Biology in press.

* Faculty of 1000

** Faculty of 1000 top 10 percent.